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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,699	02/22/2005	Peter C.M. Van Zijl	PKRZ 2 00816 US	7645

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EXAMINER	
ABRAHAM, SALIEU M	

ART UNIT	PAPER NUMBER
3768	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,699	VAN ZIJL ET AL.	
	Examiner	Art Unit	
	SALIEU M. ABRAHAM	3768	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,12-16,18-20,22-24 and 29-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *32-34* is/are allowed.

6)☒ Claim(s) *1-5, 12-16, 18-20, 22-24 and 29-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-5, 12-16, 18-20, 22-24 and 29-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. ***This a new matter rejection***.

3. All claims (depending from and to include independent claims 1 and 23) make recitations to an MR method to determine microvascular blood volume change(s) "***without the use of exogenous contrast or endogenous paramagnetic contrast using the parenchymal tissue siqnal***." There is no specific disclosure in the specification to support the (double negative) limitation "without the use of endogenous or exogenous contrast". While applicant's disclosure does specifically describe using a blood nulled signal for image contrast instead of endogenous or exogenous contrast agents, there is no disclosure that encompasses/specifically uses the amended claim language as recited (e.g. one which precludes the proposed method from being used in combination with or addition to such contrasts methods at different times for instance). In addition, the specification does not support determining microvascular blood volume

based upon a parenchymal tissue signal *per se* (***see response to applicant arguments***), but rather all tissue in a targeted site in which the ***blood signal*** has been ***substantially nulled/reduced*** (***see section 0011 in instant application***). For example, there is no description of other/non-parenchymal tissue signals being suppressed or reduced along with the blood signal and as such the claim as amended changes the scope of the original claim.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-5, 12-16, 18-20 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

6. In the instant claims recitation is made to an MR method for determining ***changes in microvascular blood volume (see preamble in independent claim 1)***, but the claim body does NOT include methods steps to support the determination of volume ***changes; rather recitation is made to the determination of a microvascular blood volume parameter*** . The omitted steps would appear to be as recited in dependent claims 13 and/or 14.

7. In light of item 5 supra, the preambles to independent claims 1 and 23 have not been accorded patentable weight because they do not "give light, meaning and vitality" to the claims as recited (***see Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165-66 (Fed. Cir. 1999)***). Specifically, the claims as

recited do not appear to require method steps to determine ***blood volume changes***. It is suggested that patentable weight subject matter be included in the main body of the claims.

Note: Examiner has interpreted blood nulling to encompass blood signal reduction as disclosed by applicant (0011) and predominantly arising from parenchymal tissue to be substantially equivalent to acquiring a MRI signal from tissue other than blood (e.g. tissue signal not limited solely to parenchymal tissue signal; see instant application 0011, 0022-0023, 0027, 0029, etc.).

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 1- 5, 12, 22 -24, 27 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Song, H. K. et al.; Multislice Double Inversion Pulse Sequence for Efficient Black-Blood MRI. MRM 47, 616-620; 2002 (**Song**).

In Reference to Claim 1

Song teaches a magnetic resonance method including:

a) performing a blood signal-reduction magnetic resonance excitation sequence that substantially nulls a magnetic resonance signal from blood; (see figure 1 and page 616) and

b) subsequent to the performing of the blood signal-reduction magnetic resonance

excitation sequence, performing a readout magnetic resonance sequence to acquire a magnetic resonance signal from tissue other than the nulled blood. (see figure 1)
c) determining a microvascular blood volume parameter based on the acquired magnetic resonance siqnal arising predominantly from parenchymal tissue (see p.617, lumen intensity/SNR in first paragraph)

In Reference to Claim 2

Song teaches: the magnetic resonance method as set forth in claim 1, wherein the performing of a blood signal-reduction magnetic resonance sequence includes:

a) performing an inversion recovery magnetic resonance excitation sequence having an inversion time to substantially reduce the magnetic resonance signal from blood. (see pages 616-617 and figure 1)

In Reference to Claim 3

Song teaches the magnetic resonance method as set forth in claim 2, wherein the performing of an inversion recovery magnetic resonance sequence includes:

a) applying an inversion radio frequency pulse; delaying for the inversion time (60); and applying an excitation radio frequency pulse. (see page 616, paragraph 2)

In Reference to Claim 4

Song teaches the magnetic resonance method as set forth in claim 3, wherein:

a) the applying of the inversion radio frequency pulse is performed without an accompanying spatially selective magnetic gradient pulse; (see page 616 and figure 1) and
b) the applying of the excitation radio frequency pulse is performed with an accompanying spatially selective magnetic field gradient pulse. (see pages 616- 617

and figure 1)

In Reference to Claim 5

Song teaches the magnetic resonance method as set forth in claim 3, wherein the performing of an inversion recovery magnetic resonance sequence further includes:

a) applying additional inversion radio frequency pulses to maintain blood in a substantially reduced condition. (see page 616, paragraph 2 and figure 1)

In Reference to Claim 12

Song teaches:

The magnetic resonance method as set forth in claim 1, further including: generating a reconstructed image from the acquired magnetic resonance signal. (see figures 4-6)

In Reference to Claim 22

Song teaches the magnetic resonance method as set forth in claim 2, wherein performing the readout magnetic resonance sequence includes performing one or more of:

a) a single-shot imaging sequence, a single-shot echo planar sequence, a multi-shot imaging sequence, a spectroscopy sequence, a multiple slice image, a one-dimensional, two-dimensional, or three dimensional spatial encoding sequence, a fractional k-space acquisition sequence, a spin echo readout sequence, and a gradient echo readout sequence. (see page 616)

In Reference to Claim 23

Song teaches a magnetic resonance system including:

a) a blood signal reduction means for performing a blood signal reduction magnetic resonance excitation sequence that substantially reduces a magnetic resonance signal from blood; (see abstract and page 616)

and

b) a readout means for performing a readout magnetic resonance sequence to acquire a magnetic resonance signal from tissue other than the nulled blood, the readout means operating subsequent to operation of the blood nulling means. (see abstract, figure 1 and page 617, paragraph 2)

In Reference to Claim 24

Song teaches the magnetic resonance system as set forth in claim 23, wherein the blood nulling means includes:

a) an inversion recovery means for performing an inversion recovery magnetic resonance excitation sequence having an inversion time (60) in which magnetic resonance of blood is substantially nulled. (see page 617 and figure 2)

In Reference to Claims 25 – 27

Song teaches the magnetic resonance system as set forth in claim 24, further including:

(**Re Claim 25**) a means for determining the inversion time based on a set of values including at least a magnetic field strength value and a repeat time value. (see figure 2

and page 617)

(**Re Claim 26**) - a means for measuring a T1 value of blood, the inversion time being obtained from the measured T1 value of blood. (see pages 617 and Discussion section on page 619)

(**Re Claim 27**) - further including: a reconstruction means for generating a reconstructed image from the acquired magnetic resonance signal. (see pages 617-619, and figures 3-6)

In Reference to Claim 31

Song teaches the magnetic resonance system as set forth in claim 27, further including: a means for combining the reconstructed image with a reference image to identify an abnormality in the reconstructed image. (see pages 617-618 and figures 3-6)

Allowable Subject Matter

9. Claims 13-16, 18-20 and 29-30 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

10. Claims 32-34 are allowed.

11. The following is a statement of reasons for the indication of allowable subject matter: the prior art was not found to anticipate or render obvious a magnetic resonance method and/or system that employs ***blood signal nulling/reduction*** along with physiological perturbations ***to assess vascular changes in blood volume*** from

(and ***requiring***) ***contrast-enhanced images generated only as a result of the nulled signal independent of other contrast agents.***

Response to Arguments/Remarks

12. Examiner acknowledges applicant's amendments to claims 1-5, 12-16, 18-19, 22-24 and 29-31, cancellation of claims 6-11, 17, 21, 25-28 and addition of new claims 32-34. Claims 1-5, 12-16, 18-20, 22-24 and 29-34 are currently pending in the instant application.

13. Examiner further acknowledges that the prior 102(b) rejections and reference to Fritz (now moot due to claim cancellation) were due to transcription errors. Examiner hereby withdraws the 102(b) rejections in the instant action. All 102 rejections have been resubmitted as 102(a) rejections to the primary reference to Song.

14. Regarding claims 1-5, 12 and 22-24, 27 and 31 Examiner asserts that the amended claim subject matter introduces new matter into the instant claims. Specifically, applicant does not disclose the specific (double negative) limitation with respect to the exogenous and endogenous contrast agents in the instant application (also see 112 1st. rejection). Further, the black-blood method of Song anticipates applicant claims because the pulse sequences and target tissue acquisitions are substantially the same as applicant's (see figs. 1-5 and p. 618, discussion of fig.6 vessel image isolation) and this method does not include using endogenous or exogenous agents to achieve anatomical target(s) image contrast. Therefore, even if language in claim (1 and 23) preamble were accorded patentable weight, the claims would not

distinguish over the prior art reference to Song.

15. Applicant's arguments with regard to claims 1-5, 12-16, 18-20, 22-24 and 29-34 filed February 18, 2008 have been fully considered and they are persuasive with respect to claims 13-16, 18-20 and 29-30 and 32-34.

16. Therefore, the rejections for claims 13-16, 18-20 and 29-31 from the prior office action filed November 19, 2007 are withdrawn and new grounds of rejection have been made in the instant action. Rejections for claims are maintained and only modified to properly recite anticipation under 35 U.S.C. 102(a). The instant Office Action is made **non-final**.

Conclusion

5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Bernard et al., Costantinides et al., Cremillieux et al., Foo et al., Kassai et al., Kojima et al., Miyazaki et al. and Weisskoff et al. have been included because they all teach the use of diagnostic magnetic resonance imaging-based methods and systems which make use of contrast-enhanced MR imaging for vascular studies similar in scope to applicant's proposed invention.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Salieu M. Abraham whose telephone number is (571) 270-1990. The examiner can normally be reached on Monday through Thursday 9:30 am - 7:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

09/10/09 SA

/Long V Le/
Supervisory Patent Examiner, Art Unit 3768